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#### REMARKS

Claims 1 and 10 are rejected as anticipated by US Patent No. 4,863,972 to Itagaki et al. (the "972 patent"). Claims 1, 5, and 8-10 are rejected as anticipated by Thanoo (J. Pharm. Pharmacol. 1993) ("Thanoo 1993"). Claims 1, 5, 8, 10, and 11 are rejected as anticipated by Thanoo (J. Applied Biomat. 1991) ("Thanoo 1991"). Claims 39-41, 44, 46, and 48-50 are rejected as anticipated by US 5,508,317 to Muller (the "317 patent"). Claims 6, 12, and 13 are rejected as obvious over either Thanoo 1991 or 1993 in view of US Patent No 6,265,509 to Muller (the "509 patent"). Claims 42, 43, 45, and 47 are rejected as obvious over the '317 patent in view of Thanoo '1991.

### The rejection of claims 1 and 10 as anticipated by the '972 patent

The '972 patent teaches crosslinking PVA with glutaraldehyde- a well-known method of crosslinking PVA. The PVA used therein does not have "pendant chains which are crosslinkable"- as recited in claims 1 and 10, it simply has hydroxyl groups. The glutaraldehyde does not form pendant groups- it simply acts as the crosslinker to join together the vinyl alcohol groups. Moreover, the '972 patent does not teach using macromers- macromolecular monomers-that are crosslinkable. This rejection is respectfully traversed.

# The rejection of claims 1, 5, and 8-10 as anticipated by Thanoo 1993 and claims 1, 5, 8, 10, and 11 as anticipated by Thanoo 1991

Both Thanoo references also teach PVA crosslinked with glutaraldehyde. The references do not teach using macromers having pendant crosslinkable chains. These rejections are respectfully traversed.

#### The rejection of claims 39-41, 44, 46, and 48-50 as anticipated by the '317 patent

Applicants acknowledge in the application that the macromers taught in the '317 patent can be used in the claimed invention. However, the '317 patent teaches that the crosslinkable groups are crosslinkable via "photocrosslinking, thermal crosslinking or 2+2 photocyclodimerization." The preferred method is photocrosslinking, which generally requires

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the use of a photoinitiator and the crosslinking is initiated by actinic or ionizing radiation. The '317 patent does not teach crosslinking via "redox initiated free radical polymerization", as recited by the claims. Accordingly, the claims are not anticipated by this reference and this rejection is respectfully traversed.

The rejection of claims 6, 12, and 13 as obvious over either Thanoo 1991 or 1993 in view of the 509 patent

This rejection is also respectfully traversed. As with the '317 patent discussed above, the '509 patent teaches moldings formed from macromers. Applicants acknowledge in the application that the macromers taught by Müller can be used in the claimed invention.

As the Examiner points out, Müller teaches that various moldings can be formed, such as "biomedical and ophthalmic mouldings, mouldings used in surgery, such as heart valves and artificial arteries, films and membranes". Such moldings are produced by introducing the prepolymer into a mould, crosslinking the prepolymer, and then removing the article from the mould.

As discussed above, the Thanoo references teach microspheres formed by polymerizing PVA with glutaraldehyde. They do not teach the use of a prepolymer (macromer). Glutaraldehyde crosslinked PVA particles have been used for a number of years. Thanoo teaches a similar material- formed into microspheres rather than irregularly shaped particles. A particular drawback of glutaraldehyde crosslinked PVA is that it forms tough, water insoluble particles (see Billmeyer, F.W. Jr; Textbook of Polymer Science', John Wiley & Son, Inc. Singapore, pp 391-395, 1984).

The '509 patent does not teach making microspheres. The moldings that are described are articles formed using a mold. Microspheres are not made this way and the reference does not suggest making microspheres. Thanoo does not suggest microspheres made by crosslinking a prepolymer- i.e. a polymer having crosslinkable groups. Thanoo teaches only crosslinking PVA polymer using glutaraldehyde. The microspheres taught by Thanoo are very different from the claimed microspheres. For one thing, by using macromers, the use of glutaraldehyde is completely avoided and the resulting microspheres do not have residual glutaraldehyde.

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There is no suggestion found in either reference to combine their teachings, as is required to maintain a rejection of obviousness.

## The rejection of claims 42, 43, 45, and 47 as obvious over the '317 patent in view of Thanoo 1991

These claims are dependent on claim 39, which was rejected as anticipated by the '317 patent. As discussed above, the '317 patent does not teach crosslinking via "redox initiated free radical polymerization", as recited by the claim 39. Thanoo 1991 also does not teach free radical crosslinking but teaches crosslinking via glutaraldehyde. Accordingly, since neither reference teaches or suggests this aspect of the invention, the claims are not obvious in view of the combination of references. This rejection is respectfully traversed.

Respectfully submitted,

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I hereby certify that this paper, along with any paper referred to as being enclosed or attached, is being faxed to the United States Patent and Trademark Office fax number (703) 872-9306 on the date shown below.

Collen A. Beard

October 21, 2004